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ORIGINAL ARTICLE

CLINICAL-EPIDEMIOLOGICAL PROFILE OF COVID-19 PATIENTS DURING THE FIRST WAVE OF THE DISEASE IN THE STATE OF PARÁ, BRAZIL

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ABSTRACT

December 2019 saw several cases of pneumonia of unknown origin reported in Wuhan, China; the cause of this unknown disease was later identified as the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The purpose of the present study was to evaluate the epidemiological profile of coronavirus disease 2019 (COVID-19) in the North Region of Brazil to assess possible correlations between demographic, social and health factors as well as adherence to safety protocols and the epidemiological profile of COVID-19. Information was obtained via a socio epidemiological survey carried out using Google Forms shared on various social media platforms from May 13 to 20, 2020. 6,781 people, living in the State of Pará, participated in the study of which only 682 (10.1%) had been diagnosed with COVID-19. Of these, 43 (6.3%) required hospitalization. 155 (23.5%) tested positive by RT-PCR associated with computed tomography. The RT-PCR test, with no association with other methods, was performed in 77 (11.6%) cases and serology performed in 360 cases (54.6%). There was a higher prevalence of confirmed cases (457, 67.0%) in females than in males, and the predominant age group was 30 to 40 years of age (214 participants, 31.4%). Considering the relatively homogeneous demographic profile of the sample, continued research is vital, preferably multi-centric studies, to obtain relevant data regarding the epidemiological dynamics of COVID-19; this data will allow the development of pandemic-prevention strategies that consider the social, cultural and political aspects of specific locations.

KEY WORDS: COVID-19; epidemiology; pandemic.

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INTRODUCTION

In December 2019, many cases of pneumonia of unknown etiology, spreading at an alarming rate, were reported to health authorities in Wuhan, China (Sun et al., 2020). Subsequently, researchers confirmed that the cause of the unknown disease was a new coronavirus, which is an RNA virus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the seventh member of the Betacoronavirus genus capable of infecting humans (Gorbalenya et al., 2020).

In January 2020, the World Health Organization (WHO) declared the SARS-CoV-2 outbreak a Public Health Emergency of International Interest (ESPII), and in March, it was declared a pandemic (Cucinotta & Vanelli, 2020; WHO, 2020a). The first case of coronavirus disease 2019 (COVID-19) in Brazil was confirmed on February 26, 2020, and the presence of COVID-19 was first confirmed in the North Region of the country on March 13, 2020, in the State of Amazonas (Rodriguez-Morales et al., 2020). In the State of Pará, the first case was confirmed on March 18, 2020 (SESPA, 2021). Data from the State Health Department shows that as of October 15, 2021, the State of Pará had reported 595,130 confirmed cases of COVID-19, with 557,526 recoveries and 16,706 deaths (SESPA, 2021). During the first wave of COVID-19, the moving average number of cases peaked on May 21, 2019, at 2,810 cases (SESPA, 2021).

Due to the rapid spread of COVID-19 in Brazil (Brazil 2020a, 2020b), clinical and epidemiological data were published daily on easily accessible media channels. Studies integrating epidemiological data from different geographic regions of Brazil are extremely important, especially since different regions are characterized by distinct and unique socio demographic characteristics. In this context, the present study describes the epidemiological scenario of COVID-19 in the state of Pará, northern Brazil, and evaluates possible associations with demographic, social, and health aspects, as well as adherence to safety protocols, to increase understanding of the pandemic in Pará during the first wave of SARS-CoV-2.

MATERIAL AND METHODS

In this cross-sectional descriptive study, a socio epidemiological survey with Google Forms was carried out using a convenience sample; the survey was shared on various social media platforms from May 13 to 20, 2020, and approved by the Research Ethics Committee of the Institute of Health Sciences (CAAE 31800720.1.1001.0018) of the Federal University of Pará. Only residents of the State of Pará who had a confirmed diagnosis of COVID-19 were selected. The socio-epidemiological characteristics were presented using descriptive statistics. Data were quantified and tabulated on Microsoft Excel version 2010 spreadsheets.

RESULTS

General characteristics of the participants

Between May 13 and 20, 2020, 6,781 residents in the State of Pará responded to the epidemiological survey. 4,690 (69.1%) participants resided in the capital city Belém (PA), and 982 (14.4%) resided in the municipality of Ananindeua (PA). Among the participants, 682 (10.1%) had tested positive to COVID-19.

Most of the participants in this study were between 20 and 29 years of age (2025; 29.9%), female (4,684; 69.1%) and married (3,170; 46.7%), regarding ethnicity/skin color the majority declared themselves brown (3871; 57.1%), as for education (2,317; 34.2%) had completed postgraduate studies, and claimed to receive five times more than the minimum wage (2,416; 35.6%).

Regarding the sex of individuals who reported a diagnosis of COVID-19, 457 (67.0%) were female, and 225 (33.0%) were male. 214 (31.4%) were between 30 and 39 years old and 35 (5.2%) were elderly, over 60 years old, and 12 (1.8%) were children and adolescents between 10 and 19 years of age.

Regarding ethnicity/skin color, 414 (60.7%) considered themselves brown, 217 (31.8%) white, 37 (5.4%) black and 14 (2.1%) yellow (Asiatic). As for marital status 425 (62.3%) claimed to be married.

Regarding education, 311 (45.6%) had completed postgraduate studies, and 154 (22.6%) were graduates. Regarding family income, 339 (49.7%) of the participants reported an income five times the minimum wage. Table 1 shows the general characteristics of participants in the survey that tested positive for COVID-19.

Diagnosis and treatment of COVID-19

Of the participants, 682/6,781 (10.1%) had tested positive to COVID-19, 1,593 (23.5%) had suspected COVID-19 and 4,506 (66.4%) were not diagnosed with COVID-19 (Table 2).

Regarding undiagnosed individuals, 4,279 (95.0%) said they had not been tested for COVID-19; while 218 (4.8%) claimed to have taken some test to diagnose the disease and nine (0.2%) did not inform. Regarding suspect cases of COVID-19, 1,040 (83.4%) individuals said they had not been tested, while 207 (16.6%) had undergone some test method.

Regarding the methods used for diagnosis, 155 (23.5%) reported being positive by RT-PCR associated with computed tomography. The RT-PCR test, with no association with other methods, was performed in 77 (11.7%) of the cases and serology performed in 360 cases (54.6%).

Table 1. General characteristics of the survey participants with diagnosis of COVID-19.

General characteristics	Total	%
Sex		
Female	457	67.0
Male	225	33.0
Age group		
10–19	12	1.8
20–29	110	16.1
30–39	214	31.4
40–49	181	26.5
50–59	130	19.0
60–69	27	4.0
70–79	6	0.9
80 years or more	2	0.3
Marital status		
Married/Stable Marriage	425	62.3
Divorced/Separated	49	7.2
Single	199	29.2
Widowed	9	1.3
Education		
Completed primary education	7	1.0
Did not complete elementary school	8	1.2
Completed high school	69	10.1
Did not complete high school	6	0.9
Completed higher education	154	22.6
Did not complete higher education	75	11.0
Completed postgraduate education	311	45.6
Did not complete postgraduate education	52	7.6
Family income		
1 minimum wage	37	5.4
2 minimum wages	69	10.1
3 minimum wages	99	14.5
4 minimum wages	81	11.9
5 minimum wages	57	8.4
More than 5 minimum wages	339	49.7

Regarding the care of positive patients, 567 (83.1%) reported that they sought and received health care, and 115 (16.9%) reported not having access to health care. Forty-three (6.3%) people reported being hospitalized, while 639 (93.7%) reported that they had not required hospitalization.

Table 2. Diagnosis and treatment of COVID-19 among the survey participants resident in the State of Pará.

Diagnosis and treatment	Total	%
Have you been diagnosed with COVID-19?		
I had a confirmed case	682	10.1
I had a suspected case	1,593	23.5
No	4,506	66.4
Where did you undergo treatment?		
At home	590	86.5
At a Field Hospital	3	0.4
At a Unified Health System (SUS) Facility	24	3.5
At a Private Hospital	31	4.6
I did not receive treatment	34	5.0
Did you go to hospital?		
No	639	93.7
Yes	43	6.3

Risk factors for COVID-19

Among the population with confirmed COVID-19, only 446 (65.4%) underwent health monitoring, 66 (9.7%) by the Unified Health System (SUS) and 398 (58.4%) by a private network.

Of the participants, 286 (42.0%) belonged to a high-risk group, while 396 (58.0%) did not belong to a high-risk group. Of the most cited risk factors, shown in Table 3, hypertension was predominant in 100 (35.0%) individuals, followed by respiratory disease in 65 (22.7%) and obesity in 59 (20.6%) people.

An important finding was that none of the 22 smokers (3.2%) who were positive for COVID-19 required hospitalization, while 42 nonsmokers (6.2%) were hospitalized.

Symptomatology

Regarding signs and symptoms from January 2020 until the time of questionnaire completion, 677 (99.3%) people reported symptoms during this period, 42 (6.2%) were hospitalized, and six (0.9%) were asymptomatic. Of

those who had shortness of breath (331, 48.5%), 39 (11.8%) were hospitalized. The most prevalent signs and symptoms are shown in Table 4.

Table 3. Risk factors for COVID-19 among participants diagnosed with COVID-19.

Risk factors	Total	%
Respiratory disease	65	22.7
Obesity	59	20.6
Hypertension	100	35.0
Cancer	5	1.7
Diabetes	12	4.2
Autoimmune disease	14	4.9
Smoking	22	7.7

Table 4. Clinical signs and symptoms reported by participants diagnosed with COVID-19.

Clinical signs and symptoms of COVID-19	Total	%
Headache	543	79.6
Loss of smell	487	71.4
Loss of taste	450	65.9
Cough	471	69.0
Sore throat	409	59.9
Diarrhea	391	57.3
Fever	388	56.8
Shortness of breath	331	48.5
Coryza	337	49.4
Nausea	235	34.4
Abdominal pain	193	28.3
Vomiting	88	12.9

487 (71.4%) people reported contact with someone diagnosed with COVID-19, while 149 (21.8%) people did not know whether they had been in contact with someone diagnosed with COVID-19. Forty-six individuals (6.7%) reported no contact with people diagnosed with COVID-19.

Protection measures against COVID-19

Table 5 shows that 612 (89.7%) people practiced social distancing. The supermarket and pharmacy were the most visited locations according to 489 (78.2%) and 448 (71.6%) individuals, respectively.

Mask were worn by 650 (93.3%) people; 609 (93.7%) reported that they wore a mask "always", and 38 (5.8%) reported that they wore a mask "sometimes" and three (0.5%) reported wearing a mask "rarely".

Table 5. Protection measures against COVID-19 reported by participants in the study.

Protection measures against COVID-19	Total	%
Did you go out during the social distancing period?		
Yes	612	89.7
No	70	10.3
If you went out, were did you go?		
Supermarket	489	78.2
Drugstore	448	71.6
Work	337	53.9
Hospital/medical appointment	240	38.4
Bank	206	32.9
Street market	122	19.5
Relative's house	50	8.0
Friend's house	16	2.5
Did you wear a mask when out?		
Yes	650	93.3
No	32	4.7
If yes, how often?		
Always	609	93.7
Sometimes	38	5.8
Rarely	3	0.5
Did you follow the hand washing recommendations?		
Many times a day	632	92.7
Only sometimes	48	7.0
Rarely	2	0.3

Regarding hand washing recommendations, 632 people (92.7%) reported that they washed their hands "several times a day", 48 participants (7.0%) reported that they washed their hands "only sometimes", and 2 (0.3%) reported that they washed their hands "rarely".

Among the 682 individuals diagnosed with COVID-19, only 112 (16.4%) did not have health insurance. Among those who had a health insurance plan, 36 (6.3%) were hospitalized, and among those without a private plan, 7 (6.2%) were hospitalized.

DISCUSSION

In the present study, females and those aged 30 to 40 years had the highest prevalence rate of COVID-19. These results are similar to those found in the State of Amapá (Silva et al., 2020) and are in line with what has been reported in the Epidemiological Bulletin of the State of Pará throughout the epidemic period (SESPA, 2021), as well as in the study by Bichara et al. (2021). These authors refer to the divergence of results observed in São Paulo (Teich et al., 2020) and in England (de Luslgnan et al., 2020), associated with the high mortality rate among men described in 37 out of 38 countries that reported data by sex (Schully et al., 2020). Authors such as Kopel et al. (2020), Gebhard et al. (2020) and Pinna (2021) emphasize that the sex factor on SARS-CoV-2 infection still needs further investigation, considering genetic, immunological, hormonal, socio-environmental, economic and lifestyle factors in the possible determination of these differences.

Most interviewees claimed to have an income of more than five minimum wages, complete postgraduate studies and the percentage of participants who reported receiving medical follow-up through the SUS was low. This profile characterizes the sample as a portion of the population with access to supplementary health services. This is corroborated by Oliveira et al. (2020), Nascimento et al. (2020) and Guibul et al. (2017). In spite of the SUS being the largest public health system in the world and playing a large role in epidemiological surveillance, most people who use are in the low-income bracket.

In the first months of the new coronavirus pandemic, when this study was carried out, Brazil did not have the budget or venues to perform mass testing; therefore, the Ministry of Health advised that only those with moderate to severe clinical conditions should be tested. For patients with mild symptoms, self-isolation was recommended (Brazil, 2020a). This testing dynamic is reflected in the results of the present study, considering the relatively low percentage of people with a confirmed COVID-19 diagnosis and with serological testing the most frequent test method among participants. Bichara et al. (2021) noted similar results.

The WHO recommends RT-PCR molecular tests to detect the viral genome of SARS-CoV-2 in respiratory tract samples. RT-PCR is the gold standard for the diagnosis of COVID-19, and chest computed tomography is the best choice for image diagnosis in cases of severe acute respiratory syndrome associated with COVID-19 (WHO, 2020a). This may explain why for most of the participants, the diagnosis was confirmed by computed tomography and RT-PCR, as this was the recommended medical approach at the time. Bichara et al. (2021) reported similar results.

Regarding clinical factors, almost half of the interviewees reported belonging to a high-risk group, where hypertension, respiratory diseases and diabetes were the most reported comorbidities among the possibilities presented. This was similar to the results of other studies in the literature (CDC COVID-19, 2020; Richardson et al., 2020; Kreutz et al., 2020). Since the beginning of the pandemic, hypertension has been closely associated with the development of severe cases of COVID-19. This association may be related to the presence of the angiotensin 2 converting enzyme (ACE2). This enzyme, which is found in large quantities in patients with hypertension and diabetes, due to the use of drugs to control these diseases, is also considered the main point of virus entry into cells. In addition, ACE2 has been directly linked to organs such as the liver, heart and pancreas (Huang et al., 2020; Wan et al., 2020).

Among the signs and symptoms reported by the study participants, headache, cough, sore throat, loss of smell and taste, diarrhea and fever were the most frequently reported, similar to other studies (Silva et al., 2020; Giacomelli, 2020; WHO, 2020b; Bichara et al., 2021), even though there is a report classifying headache as a less frequent symptom (Zhu et al., 2020). Thus, it is worth noting that the referred signs and symptoms may vary according to the stage of the disease. Moreover, many people are considered asymptomatic, demonstrating that clinical characteristics, in many cases, are variable (Iser et al., 2020).

Regarding adherence to safety protocols during the COVID-19 epidemic, most participants reported practicing social distancing. Findings described by Bezerra et al. (2020) indicated that people who partially or totally isolated themselves believed that social distancing helped reduce the number of cases of COVID-19, preventing the spread of the virus by asymptomatic victims (Wilder-Smith & Freedman, 2020).

Although a large part of the studied population claimed to practice social distancing, a high percentage reported having had contact with people who had been diagnosed with COVID-19. This may be related to the fact that even among people who practiced social distancing, some daily activities, such as going to the supermarket or the pharmacy, led to contact with other people, which certainly favored exposure to the virus. Therefore, the recommendations for social distancing must always take into account the social, cultural and

political characteristics of a particular population at the time of the pandemic (Aquino et al., 2020).

Most participants in this study claimed to use masks and practice hand hygiene, similar to the results of a study by Costa-Lima et al. (2020). Although some sectors of society question the effectiveness of wearing masks as a way of protecting against SARS-CoV-2, mask wearing is the WHO official recommendation and that of the Brazilian Ministry of Health. Further studies are necessary to demonstrate the effectiveness of this prevention method (Brazil, 2020b; Garcia, 2020).

The results of this study highlight that during the first epidemiological wave of the COVID-19 pandemic in Belém-PA, all safety protocols recommended by national and international health institutions regarding diagnosis, treatment, and prevention methods were generally reported as being followed. However, the social isolation index of 53%, as reported by the Government of the State of Pará in response to the confinement decree (lockdown) imposed on the population of Belém in April 2020, did not reach the expected minimum of 70%. This suggests that even though this population generally followed the guidelines for social isolation, daily life needs influenced adherence during the period that preceded data collection in this study, showing that if isolation recommendations are not conceived in compliance with the cultural and sociopolitical particularities of each location, the expected end result will not be achieved.

The fact that the study was carried out at the beginning of the pandemic period and that the questionnaire was applied online can be seen as factors that can influence the veracity of the responses obtained, since at the time of the research very little was known about the new coronaviruses and COVID-19. The lack of accurate information at the time on modes of transmission, prevention, diagnosis and treatment favored the proliferation of false news, with many questions arising every day. We understand that the complexity of the epidemic, together with the absence of precise information about the socio-epidemiological aspects of COVID-19, may have influenced the investigated public's responses to the questionnaire, which can be considered a limitation in the present study.

Considering the relatively homogeneous demographic profile of this sample, it is important that further research be carried out, preferably multi-centered studies, to obtain relevant data on the epidemiological dynamics of COVID-19 and, based on the information obtained, design more effective prevention strategies considering the social, cultural and political particularities of each location.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest

REFERENCES

1. Aquino EML, Silveira IH, Pescarini JM, Aquino R, de Souza-Filho JA, Rocha AS, Audêncio AF, Teixeira VC, Machado DB, Paixão E, Alves FJO, Pilecco F, Menezes G, Gabrielli L, Leite L, de Almeida MCC, Ortelan N, Hapuk Q, Fernandes RF, Flores RJ, Palmeira ORN, Pinto Junior EP, Aragão E, de Souza LEPF, Barral Netto M, Teixeira MG, Barreto ML, Ichihara MY, Lima RTRS. Medidas de distanciamento social no controle da pandemia de COVID-19: potenciais impactos e desafios no Brasil. *Cien Saude Colet 25*: 2423-2446, 2020.
2. Bezerra ACV, Menezes da Silva CE, Soares FRG, da Silva JAM. Fatores associados ao comportamento da população durante o isolamento social na pandemia de COVID-19. *Cien Saude Colet 25*: 2411-2421, 2020.
3. Bichara CDA, da Silva Graça Amoras E, Vaz GL, da Silva Torres MK, Queiroz MAF, do Amaral IPC, Vallinoto IMVC, Bichara CNC, Vallinoto ACR. Dynamics of anti-SARS-CoV-2 IgG antibodies post-COVID-19 in a Brazilian Amazon population. *BMC Infect Dis 21*: 443, 2021.
4. Brasil. Ministério da Saúde. *Plano de Contingência Nacional para Infecção Humana pelo Novo Coronavírus - COVID-19*. Centro de Operações de Emergências de Saúde Pública Brasília, 2020a. Available in: https://www.gov.br/saude/pt-br/coronavirus/publicacoes-tecnicas/guias-e-planos/livreto-plano-de-contingencia-espin-coe-26-novembro-2020 Access in: 15.fev.2021
5. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. *Guia de Vigilância Epidemiológica para Infecção Humana pela COVID-19.* Brasília: Ministério da Saúde, 2020b. Available in: https://www.gov.br/saude/pt-br/coronavirus/publicacoes-tecnicas/guias-e-planos/guia-de-vigilancia-epidemiologica-covid-19/view Access in: 15.fev. 2021.
6. CDC COVID-19 Response Team. Preliminary Estimates of the Prevalence of selected Underlying Health Conditions among Patients with Coronavirus Disease 2019 - United States, February 12-March 28, 2020. *Morb Mortal Wkly Rep 69*: 382-386, 2020.
7. Costa-Lima MF, Mambrini JVM, Andrade FB, Peixoto SWV, Macinko J. Distanciamento social, uso de máscaras e higienização das mãos entre participantes do Estudo Longitudinal da Saúde dos Idosos Brasileiros: iniciativa ELSI-COVID-19. *Cad Saúde Pública 36*: 3, 2020.
8. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. *Acta Biomed 91:* 157-160, 2020.
9. Garcia LP. Uso de máscara facial para limitar a transmissão da COVID-19. *Epidemiol Serv Saúde 29*: 2, 2020.
10. Gebhard C, Regitz-Zagrosek V, Neuhauser HK, Morgan R, Klein SL. Impact of sex and gender on COVID-19 outcomes in Europe. *Biol Sex Differ 11:* 29, 2020.

11. Giacomelli A, Pezzati L, Conti F, Bernacchia D, Siano M, Oreni L, Garcia LP. Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. *Clin Infect Dis 71:* 889-890, 2020.

12. Gorbalenya AE, Baker SC, Baric R, Groot RJ, Drosten C, Gulyaeva AA, Haagmans BL, Lauber C, Leontovich AM, Neuman BW, Penzar D, Perlman S, Poon L, Samborskiy D, Sidorov IA, Solá Gurpegui I, Ziebuhr J. Severe acute respiratory syndrome-related coronavirus: the species and its viruses a statement of the Coronavirus Study Group. *Nat Microbiol 5:* 536-544, 2020.

13. Guibul IA, de Moraes JC, Guerra Junior AA, Costa EA, Acurcio FA, Costa KS, Karnikowski MGO, Soeiro OM, Leite SN, Álvares J. Características principais dos usuários dos serviços de atenção primária à saúde no Brasil. *Rev Saúde Pública 51*: 17, 2017.

14. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet 395*: 497-506, 2020.

15. Iser BPM, Moehlecke BP, Sliva II, Timmen V, Poleto RMB, Schuelter-Trevisol F, Bobinski F. Definição de caso suspeito da COVID-19: uma revisão narrativa dos sinais e sintomas mais frequentes entre os casos confirmados. *Epidemiol Serv Saúde 29:* 3, 2020.

16. Kopel J, Perisetti A, Roghani A, Aziz M, Gajendran M, Goyal H. Racial and Gender-Based Differences in COVID-19. *Front Public Health 28*: 8:418, 2020.

17. Kreutz R, Algharably EAE, Azizi M, Dobrowolski P, Guzik T, Januszewicz A, Persu A, Prejbisz A, Riemer TG, Wang JG, Burnier M. Hypertension, the renin-angiotensin system, and the risk of lower respiratory tract infections and lung injury: implications for COVID-19. *Cardiovasc Res 116*: 1688-1699, 2020.

18. Nascimento LC, Viegas SMFV, Menezes C, Roquini GR, Santos TR. O SUS na vida dos brasileiros: assistência, acessibilidade e equidade no cotidiano de usuários da Atenção Primária à Saúde. *Physis 30*: 3, 2020.

19. Oliveira WK, Duarte E, França GVA, Garcia LP. Como o Brasil pode deter a COVID-19. *Epidemiol Serv Saúde 29*: e2020044, 2020.

20. Pinna G. Sex and COVID-19: A Protective Role for Reproductive Steroids. *Trends Endocrinol Metab 32*: 3-6, 2021.

21. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW; the Northwell COVID-19 Research Consortium, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, Hirschwerk DA, Kim EJ, Kozel ZM, Marrast LM, Mogavero JN, Osorio GA, Qiu M, Zanos TP. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA 323:* 2052-2059, 2020.

22. Rodriguez-Morales AJ, Gallego V, Escalera-Antezana JP, Méndez CA, Zambrano LI, Franco-Paredes C, Suárez JA, Rodriguez-Enciso HD, Balbin-Ramon GJ, Savio-Larriera E, Risquez A, Cimerman S. COVID-19 in Latin America: The implications of the first confirmed case in Brazil. *Travel Med Infect Dis 35*: 101613, 2020.

23. Scully EP, Haverfield J, Ursin RL, Tannenbaum C, Klein SL. Considering how biological sex impacts immune responses and COVID-19 outcomes. *Nat Rev Immunol 20*: 442-447, 2020.

24. SESPA, Secretária de Saúde Pública Governo do Estado do Pará. *Boletim Epidemiológico do Coronavírus no Estado do Pará*. Available in: https://www.covid-19.pa.gov.br/#/ Access in: 15.out.2021

25. Silva AWC, Cunha AA, Alves GC, Corona RA, Dias CAGM, Nassiri R, Vedovelli S, Vilhena TRF, Favacho VBC, Sousa JF, Araújo MHM, Oliveira E, Dendasck CV, Fecury AA. Perfil epidemiológico e determinante social do COVID-19 em Macapá, Amapá, Amazônia, Brasil. *Rev Cient Mult Núcleo Conhec 4:* 05-27, 2020.

26. Sun P, Lu X, Xu C, Sun W, Pan B. Understanding of COVID-19 based on current evidence. *J Med Virol 92:* 548-551, 2020.

27. Teich VD, Klajner S, Almeida FAS, Dantas ACB, Laselva CR, Torritesi MG, Canero TR, Berwanger O, Rizzo LV, Reis EP, Cendoroglo Neto M. Epidemiologic and clinical features of patients with COVID-19 in Brazil. *Einstein (Sao Paulo) 18*: eAO6022, 2020.

28. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *J Virol 94:* e00127-20, 2020.

29. WHO. World Health Organization. *Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)*. 2020b. Available in: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf. Access in: 01.mar.2021.

30. WHO. World Health Organization. *Coronavirus disease 2019 (COVID-19): Situation Report -38*. 2020a. Available in: https://apps.who.int/iris/handle/10665/331226 Access in: 27.fev.2021

31. Wilder-Smith A, Freedman DO. Isolation, quarantine, social distancing and community containment: pivotal role for old-style public health measures in the novel coronavirus (2019-nCoV) outbreak. *J Travel Med 27*: taaa020, 2020.

32. Zhu J, Zhong Z, Ji P, Li H, Li B, Pang J, Zhang J, Zhao C. Clinicopathological characteristics of 8697 patients with COVID-19 in China: a meta-analysis. *Fam Med Community Health 8:* e000406, 2020.